REMARKS

The document is submitted in response to the Office Action dated December 17, 2009 ("Office Action"). Applicants have amended claim 9 to include a number of limitations recited in claim 20, support for which was addressed in Applicants' response filed on October 1, 2009. No new matter is added.

Upon entry of the proposed amendments, claims 1, 3-10, 12, and 14-21 will be pending and under examination. Applicants respectfully request that the Examiner reconsider this application in view of the following remarks.

35 U.S.C. § 102 Rejections

The Examiner rejected claims 1, 3, 7-10, 12, 16-18, and 20-21 for anticipation under §102(b) by WO00/54876 by Bormann *et al.* ("Bormann"). See the Office Action, page 2, item 3. Applicants respectfully traverse, discussing independent claim 1 first.

Claim 1 is drawn to a filter device for the depletion of the leukocyte content from a blood product. The filter includes a housing having an inlet and an outlet. Within the housing, more than two porous elements are configured to remove leukocytes. Each of the porous elements includes one or more layers of a filtering material and each of the porous elements has a different hydrophilicity. The more than two elements are arranged in the filter device such that **any** of the porous elements has a higher hydrophilicity than a **successive** porous element in a direction of flow, from the inlet to the outlet, of the blood product through the filter device. In other words, a negative hydrophilicity gradient exists between the two porous elements and along the direction of the flow.

According to the Examiner, Bormann "discloses a filter device for the depletion of the leukocyte content from blood products ... comprising the features of a housing ... with an inlet (20) [port] and an outlet (20) port and within the housing, more than two porous elements." See the Office Action, page 2, lines 10-13, emphasis added. The Examiner then asserted that the two porous elements have a "different hydrophilicity ... wherein the first porous element has a different hydrophilicity than the successive filter elements." As such, the Examiner concluded that "it is implicit that the difference is [the] first porous element (closer to the inlet) has a higher hydrophilicity than the

successive elements in the direction of flow, from inlet to outlet." See the Office Action, page 2, lines 7-15, emphases added. To support this assertion, the Examiner referred to page 12, lines 5-15; page 12, lines 6-9; page 11, lines 5-28; and FIGs. 1-3 of Bormann. Applicants disagree.

I

Initially, Applicants would like to point out that, in claim 1, the negative hydrophilicity gradient between **any** two porous elements has a particularly required direction. That is, the hydrophilicity decreases along the direction of the flow from the inlet to the outlet. It does not equal the Bormann "difference," which does not entail such a particular direction required in claim 1. Indeed, the passages referred to by the Examiner merely teach that there is a hydrophilicity difference between two specified elements. They do not teach or suggest the direction particularly required in claim 1, i.e., a negative hydrophilicity gradient between **any** two elements, where the element closer to the inlet has a higher hydrophilicity.

To the contrary, Applicants note that Bormann suggests a filter having no hydrophilicity direction or having a hydrophilicity direction opposite to that required in claim 1. For example, Figure 3 of Bormann shows a filter. According to related description in Example 4, alternating membranes are used in the filter and, the CWST alternates between low (65 dynes/cm) and high (95 dynes/cm) CWST. As a result, the element closest to the inlet and the element closest to the outlet have the same CWST. It follows that no hydrophilicity direction or gradient is present, let alone a negative gradient required in claim 1. Similarly, Figure 2 of Bormann shows a filter where the flow first encounters an element with a low CWST, then an element with a high CWST, then again an element with a low CWST. Again, in Figure 2, the element closest to the inlet and the element closest to the outlet also have the same CWST. It again follows that no hydrophilicity direction or gradient is present, let alone a negative gradient required in claim 1. Finally, in Figure 1 of Bormann, the order of porous filter elements is such that that the flow first encounters an element with low CWST, then an element with a high CWST. This is evidenced by Bormann's teaching that the first element (which is closer to the inlet) "can have a CWST in the range from about 58 dynes/cm to about 75

dynes/cm" and the second element "can have a CWST in the range from about 78 dynes/cm to about 115 dynes/cm" See page 12, lines 5-9. That is, the first element is less hydrophilic than the second element. This direction directly opposes to the direction required in claim 1.

Thus, to the extent that Bormann suggests a filter has no hydrophilicity direction or a hydrophilicity direction opposite to that required in claim 1, it does not anticipate the filter device of claim 1. Further, it teaches one skilled in the art away from the filter device of claim 1.

II

As mentioned above, in supporting the §102(b) rejection, the Examiner alleged implicit or inherent characteristics of the Bormann filter. See the Office Action, page 2, lines 7-15, (emphases added).

Applicants respectfully traverse. According to MPEP 2112 IV,

> The fact that a certain ... characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic [citation omitted] ... To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. ... "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." [citation omitted] ... "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species.
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> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

Here, as discussed in Part I above, there is no "evidence [that] make[s] clear that [a negative hydrophilicity gradient] is necessarily present in the thing described in [Bormann]." Also, Bormann "does not inherently disclose all species within that broad category," such as a filter device having the above-mentioned a negative hydrophilicity gradient. In addition, contrary to the MPEP's clear guidance and the holding in *Ex parte*

Levy, "the examiner [did not] provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Thus, it is submitted that the Examiner's reliance on inherent characteristics of the Bormann filter is untenable.

In view of the above remarks, Applicants submit that claim 1 is novel over Bormann. Like claim 1, independent claims 9 and 20 also require the above-mentioned negative hydrophilicity gradient. Thus, for at least the same reasons, claims 9 and 20 are also novel over Bormann. So are claims 3, 7, 8, 10, 12, 16-18, and 20-21, all of which depend from claim 1 or 20, directly or indirectly.

For a complete record, Applicants now discuss claim 8. Claim 8, dependent from claims 1 and 7, is drawn to a filter device having porous elements that have a construction of fibers of a specific polymeric material that is coated with a hydrophilic polymer. Citing page 14, lines 13-19 of Bormann, the Examiner alleged that Bormann discloses a hydrophilic polymer coating, wherein the polymer is an acrylic polymer. See the Office Action, page 4, lines 6-7.

Applicants note that this passage of Bormann, relating to a second filter element, specifies that the second filter element is provided with a hydroxylated surface. It is known in the art that hydroxylation of a surface naturally increases the CWST (i.e. hydrophilicity). Thus, the second filter element would be *more hydrophilic* than the first filter following this treatment. This embodiment therefore conflicts with the teaching of the present application, which specifies that the first filter element is *more hydrophilic* than the second filter element. Moreover, this interpretation of Bormann by the Examiner seems to ignore the context of the above cited passage, which is directed to a filter element useful for the removal of complement fragments and not for depleting leukocyte content from a blood product as present claim 1 requires. Thus, it is submitted that claim 8 is novel over Bormann on this independent ground.

35 U.S.C. § 103 Rejections

The Examiner rejected claims 1, 3-10, 12, and 14-21 for obviousness on a number of grounds. Applicants will address each of them below.

I

The Examiner rejected claims 1, 3, 7-10, 12, 16-18, and 20-21 for obviousness over the above-discussed Bormann with further evidence from EP 0542655 by Majurel ("Majurel"). See the Office Action, page 2, item 3.

Applicants respectfully traverse. As discussed above, Bormann, the primary reference, does teach or suggest the direction particularly required in claim 1, i.e., a negative hydrophilicity gradient, where the element closer to the inlet has a higher hydrophilicity. To the contrary, Bormann suggests a filter has no hydrophilicity direction or a hydrophilicity direction opposite to that required in claim 1. Therefore, Bormann teaches one skilled in the art away from the filter device of claim 1. Majurel, the secondary reference, does not rectify these defects of Bormann. More specifically, Majurel does not state that hydrophobicity is increased in order to achieve a specific technical effect. It is **silent** regarding any possible technical advantages associated with a filter hydrophilicity gradient like the one required in claim 1. Thus, the two references, alone or in combination, do not render claim 1 obvious.

In addition, Applicants would like to point out that the device of claim 1 is used for depletion of the leukocyte content from a blood product. In contrast, Majurel is from the technical field of agglutination serology, and describes techniques/devices relating to agglutination disorders and determining blood groups (also agglutination-based). In the Majurel methods, erythrocytes are **deliberately agglutinated** before application to the described filter (*see* page 2, col. 1, lines 1-5 and page 3, col. 1, lines 44-48).

In particular, Majurel does not teach a *leukocyte* depletion filter; the disclosed filter does not even appear to be suitable for filtering/removing leukocytes from a blood sample, because, according to Majurel, only agglutinated erythrocytes are retained, while the rest of the sample applied to the device (the mobile phase or "Ia phase mobile") is removed (*see* page 2, col. 2, lines 40-42 and page 3, col. 1, lines 22-29). Since Majurel is restricted to the separation of agglutinated erythrocytes from the mobile phase, and since leukocytes are not even addressed, one skilled in the art would conclude that the Majurel device is not suited for the removal of leukocytes. In sum, an increased efficiency of leukocyte removal is not taught nor suggested as the Examiner alleged. Instead, to the

extent that Majurel shows that agglutinated erythrocytes are separated from a blood sample, but the leukocytes remain in that blood sample following filtration, Majurel also teaches one skilled in the art away from the filter device of claim 1.

In view of the above remarks, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness.

Even if a *prima facie* case of obviousness were established, which the Applicants does not concede, it can be successfully rebutted by a showing of an unexpected property of the claimed method as compared with the closest prior art method. See MPEP 716.01(a) and 716.02(e) I.

Here, for example, the Majurel device and filter offers a solution suitable for micro-scale experiments only. Indeed, the described capillary in the Majurel device is only 6 cm long and 2 mm wide, *see* p. 3, col. 3, 1st paragraph; in the Examples, only 50 µl volumes are applied. In contrast, a filter device covered by claim 1 in the present application was successfully used to process a sample of as much as 450 cm^3 in volume. See Examples 1-3 in the Specification.[1] In other words, a filter device covered by claim 1 can process a blood sample of a volume that is about 9,000 times greater than that processed by the Majurel device. In short, a showing of these unexpected properties has successfully rebutted the obviousness rejection.

For the reasons and facts set forth above, Applicants submit that claim 1 is non-obvious over Bormann in view of Majurel. As discussed above, claims 3, 7-10, 12, 16-18, and 20-21 12 and 20-21 also require the negative hydrophilicity gradient. For at least the same reasons, these claims are also not rendered obvious by the cited references.

II

The Examiner rejected claims 4 and 5 for obviousness over Bormann in view of US Patent No. 4925572 to Pall ("Pall"). See the Office Action, page 5, item 4.

Claims 4 and 5 depend from claim 1. As discussed above, Bormann does not render claim 1 obvious. Here, Pall does not rectify the defects of Bormann. Thus,

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[1] Rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995),

Applicants submit that Bormann and Pall, alone or in combination, do not render claims 4 and 5 obvious.

Again, for a complete record, Applicants will address the Examiner's specific ground for rejecting claims 4 and 5.

Claim 4, dependent from claims 1 and 3, is drawn to a filter device where each of the above-mentioned porous element includes at least two adjacent layer of a specific filtering material. These at least two adjacent layers of filtering material have a construction of a same material having identical hydrophilicity properties.

The Examiner admitted that Bormann does not disclose that the filter layers are made of the same material, and thus "have the same hydrophilicity properties." Yet, she stated that Pall describes "the use of multiple layers in a filter element made of the same material, and the material inherently having the same hydrophilicity properties, absence evidence to the contrary." To support this statement, the Examiner referred to col. 28, lines 7-14 of Pall. See the Office Action, page 5, lines 13-15.

Applicants respectfully traverse. When the full context of the just-mentioned passage of Pall is considered, it is clear that this passage describes filter layers that are intended for use in a **second filter element only** of the Pall filter, which is not designed for the removal of leukocytes, but for the removal of aggregates that form in PRC (packed red cells). See col. 28, lines 4-6. Thus, the passage does not support the Examiner's statement.

Claim 5, also dependent from claims 1 and 3, specifies that the at least two adjacent layers have a decreasing pore size from the inlet to the outlet. According to the Examiner, Pall discloses that adjacent layers can have a decreasing pore size filter elements. See the Office Action, page 5, lines 18-20. Applicant would like to point out that Pall describes that several filter elements have different pore sizes, but not that at least two layers within one filter element have different pore sizes decreasing from inlet to outlet as required in claim 5. Indeed, Pall (at col. 9, lines 50-59) teaches:

The subject invention provides a device for the depletion of the leukocyte content of a blood product comprising at least first, second, and third preformed porous elements with the second element interposed between the first and third elements, each successive element having a smaller pore diameter than that preceding it, the first element including means for removing gels, the second element including means for removing microaggregates, and the third element including means for removing leukocytes.

Clearly, Pall describes that the pore diameter decreases as the filtrate moves from the first element to the third element, but not within the element itself. Also, Pall describes three porous elements, but only the third is actually used for removing leukocytes. Accordingly, at best, Pall teaches that the porous element used for leukocyte removal, i.e., the third element, has only one single pore diameter. It does not teach or suggest the limitation in claim 5, i.e., two layers within one filter element have different pore sizes decreasing from inlet to outlet.

In view of the above remarks, Applicants submit that claims 4 and 5 are non-obvious over Bormann in view of Pall on these independent grounds.

III

The Examiner rejected claim 6 for obviousness over Bormann in view of US Patent No. 5298165 to Oka *et al.* ("Oka"). See the Office Action, page 6, item 5. She also rejected claims 14, 15, and 19 for obviousness over Bormann in view of US Patent No. 5190657 to Heagle *et al.* ("Heagle"). See the Office Action, page 6, item 6.

Applicants respectfully traverse. All of claims 6, 14, 15, and 19 depend from claim 1. As discussed above, Bormann does not render claim 1 obvious. Here, neither Oka nor Heagle rectifies the defects of Bormann. Thus, the three references, alone or in combination, do not render claim 6, 14, 15, or 19 obvious.

In addition, Applicants would like to point out that claim 19 covers a filter device having gel filtration elements or microaggregate filtration elements. Referring to col. 14, lines 9-16 of Heagle, the Examiner rejected claim 19, stating that Heagle describes a *"microaggregate filtration element."* See the Office Action, page 7, line 5. Applicants

disagree and note that Heagle does not even mention the word "microaggregate" in the passage, or its entirety. The passage cited by the Examiner merely describes a pre-filter "used to remove large agglomerates and the like" i.e. macroaggregates, which are contrary to microaggregate as recited in claim 19. Thus, claim 19 is patentable over the cited references on this independent ground.

For the reasons and facts set forth above, Applicants submit that all pending claims are non-obvious over the cited references. It is respectfully requested that the rejections be withdrawn.

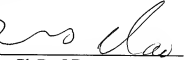
Conclusion

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

The Petition for Extension of Time fee in the amount of $130 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 50-4189, referencing Attorney Docket No. 7B901-002US1.

Respectfully submitted,

Date: 4-9-2010



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